EDITORIAL

Viral Infection of the Fetus

THE HOPE that a significant reduction in the numbers of children with congenital anomalies or mental retardation can be achieved by protecting mothers from various virus infections during pregnancy is rapidly fading, as is pointed out by the participants in the Specialty Conference elsewhere in this issue of THE WESTERN JOURNAL OF MEDICINE. The case against rubella is clear although even in this situation there is increasing pessimism about the efficacy of vaccine as a deterrent. Congenital cytomegalovirus (CMV) infection is responsible for congenital malformations but the frequency, the associated factors which influence the probability of damage to the infant following maternal CMV infection and the method for control of CMV infection in pregnant women have not been elucidated. Other agents such as herpes simplex, the enteroviruses, mumps, varicella or the poxviruses may be associated with congenital defects or intrauterine infections but such occurrences appear to be infrequent. Careful study in both humans and animals of how viral infection during pregnancy may affect offspring has led to discovery of the less obvious sequelae of fetal virus infection and the description of "expanded clinical syndromes." The mechanisms by which some of these changes are brought about remain to be determined. In the Specialty Conference, St. Geme reviews possible explanations for growth retardation, neurologic damage and the interesting immunologic differences between acquired and congenital infection with CMV or rubella.

Yamauchi discusses the difficult problem of prevention or control of fetal infection and emphasizes the concern that inapparent infection in an immunized woman *may* lead to fetal damage although such an event has *not* been documented. Experiences reported by several investigators[1,2] show that infection of immunized individuals can occur as indicated by local virus replication and boosts in antibody titers but viremia has not been demonstrated. I would suggest that rather than *not* use the existing rubella vaccines because of the possibility of reinfection at some later date, the vaccine be administered not only to the young female population but under proper circumstances to a larger proportion of the susceptible women of child-bearing age. Booster immunizations can be provided at whatever interval is necessary to preclude the likelihood of viremia occurring following infection with the wild virus. The other alternative is not to use the vaccine and thus permit pregnant women to take their chances with the wild virus. Attempts to develop a vaccine that will confer long-lasting protection should be continued but available preparations should *not* be discarded in the meantime.

Control of CMV infection and its effect on the fetus is far more difficult. The isolation of CMV or even serologic evidence of a rise in specific antibody during pregnancy are not valid indications for terminating pregnancy until we can define the factors other than infection during pregnancy that determine if the fetus will be damaged. Studies that Nankervis, Kumar, Cooper and I are now carrying forward are cited to illustrate this point, although the work of many other investigators could also be used.

In a study of a population of over 1,000 young pregnant women and the products of their gestation, 16 percent of whom presented during the first trimester and 50 percent during the second trimester, it was observed that 11 percent excreted CMV in their urine on one or more occasions but that only 10 percent of these mothers delivered babies with CMV infection. None of these infants had congenital anomalies and all were clinically well. Follow-up of these infants has not been sufficient to determine whether development remains normal, but study of similar groups by the same investigators suggests that approximately 10 percent of such infants may eventually show signs of mental or motor retardation or neurologic deficit of some kind. Thus in studies of young mothers of low socio-economic status, approximately 1 in 1,000 deliver an infant infected at birth with CMV who at some time *may* show evidence of nervous system or other

abnormality. Most infants with congenital CMV infection do well.

The factors which determine which baby is born with overt evidence of cytomegalic inclusion disease (CID) or which baby develops later complications cannot be defined. There is evidence that primary CMV infection during pregnancy is more hazardous to the infant than recurrent infection, and it has been suggested that the trimester of the primary maternal infection influences the probability of effect on the fetus. Fiala states ". . . the most severe form of cytomegalovirus infection of fetus [is] probably acquired during the first 20 weeks of pregnancy . . . " Evidence to support this idea is difficult to obtain. Mims,[3] for example, contrasts CMV with rubella, pointing out that malformation of eye, ear and heart are not recorded for CMV and that with the exception of small body size, the abnormalities in CID can be classed as lesions rather than malformations and suggests that the fetus with CID is infected at a later stage of development than is the case with rubella. Haymaker,[4] studying a newborn with CID and periventricular calcification, suggested that infection took place during the fifth month of gestation. Nankervis and collaborators[5] were able to follow eight women who had documented asymptomatic primary CMV infection during pregnancy; one in the first trimester, four in the second trimester and three in the third trimester. The woman with primary CMV in the first trimester had CMV-positive blood cultures during the first and second trimesters and positive urine, throat and cervical cultures throughout pregnancy but delivered a normal, non-infected infant. The three infants born to mothers who acquired infection during the third trimester and one of the four infants born to second trimester converters had congenital CMV infection but all infants were clinically normal. Obviously, studies of this kind must be continued until "affected" babies are observed, but there is the indication that primary CMV *late* in pregnancy may carry an increased risk of congenital infection.

The sporadic occurrence of most viral infections during pregnancy may make it difficult to show by the crude epidemiologic approaches generally used that there is an association between anomalies and intrauterine infection with various agents. Laboratory investigation of the pathogenesis of virus-induced congenital defects may provide clues as to how studies in man may be made more sensitive. For the present, rubella vaccine should be employed to minimize the occurrence of the one virus infection that is known to produce anomalies. Studies of CMV must be continued to determine how important this agent is as a cause of mental retardation or congenital malformation and if control measures are feasible.

ELI GOLD, MD
Department of Microbiology
University of the West Indies
Kingston, Jamaica, WI

REFERENCES

1. Wilkins J, Leedom JM, Portnoy B, et al: Reinfection with rubella virus despite live vaccine induced immunity: Trials of HPV-77 and HPV-80 live rubella virus vaccines and subsequent artificial and natural challenge studies. Am J Dis Child 118:275-294, 1969

2. Horstmann DM, Liebhaber H, LeVouvier G, et al: Rubella reinfection of vaccinated and naturally immune persons. N Engl J Med 283:771-778, 1970

3. Mims CA: Pathogenesis of viral infections of the fetus. Progr Med Virol 10:194-237, 1968

4. Haymaker W, Girdany BR, Stephens J, et al: Cerebral involvement in generalized cytomegalic disease in the newborn. J Neuropathol Exp Neurol 13:562-586, 1954

5. Nankervis GA, Kumar ML, Gold E: Primary infection with cytomegalovirus during pregnancy. Abstract submitted to Soc Ped Res 1974

National Health Insurance — Are We Really Ready for It Yet?

IT APPEARS to be generally accepted that this nation should have some form of national health insurance. The arguments in favor of it and the arguments against it are well known, and have worn thin. The issue is no longer whether or not, but rather it is *what* and *when.* It is disturbing to observe that there is little evidence of any real consensus as to the *what.* As to *when,* one hears that national health insurance will certainly be enacted this year, or not until next year, or not before the 1976 Presidential election. Given these uncertainties it seems reasonable to ask if we are really ready for it yet.

The record of federal intervention in health care over the last decade has not been very impressive in terms of what has been achieved to improve the nation's health. Massive programs have been imposed, often without any real discussion or advice from those most directly concerned. They turned out to be enormously expensive and have created more problems than they have solved. It seems reasonable to be appre-